



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

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MEMORANDUM

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

Subject: CGA-154281: ID Number 7E03489; Record Number 229240; Action Code  
212; Caswell No. 298C *Ref. 8-1049*

From: John H.S. Chen, D.V.M. *John H.S. Chen 11/7/88*  
Review Section I  
Toxicology Branch II  
Health Effects Division (TS-769C)

To: Kerry B. Leifer, PM 45  
Registration Support and Emergency Response Branch  
Registration Division (TS-769C)

Thru: Quang Q. Bui, Ph.D., Section Head *Quang Q. Bui 11/7/88*  
Review Section I  
Toxicology Branch II  
Health Effects Division (TS-769C) *Manufact 11/8/88*

Actions Requested:

1. Review and evaluation of the dermal absorption study with simulated metolachlor 7.8 EC formulated product containing  $^{14}\text{C}$ -CGA-154281;
2. Review and evaluation of the repeated Ames assays with CGA-154281 technical recommended by the Toxicology Branch (TB MEMO 3/14/88 and 8/19/88 J. Chen).

Recommendation:

1. The Registrant should be apprised of the deficiencies reported in the dermal absorption study with simulated metolachlor 7.8 EC formulated product containing  $^{14}\text{C}$ -CGA-154281. Ciba-Geigy Corp., Biochemical Dept. Study No. ABR-87086, December 17, 1987.
2. The following confirmatory gene mutation studies with CGA-154281 technical (Lot No. FL870211) in Ames assay were considered adequate and acceptable:
  - A. Salmonella/Mammalian-microsome mutagenicity test with CGA-154281 technical (Lot No. FL870211; Acetone as solvent). Ciba-Geigy Limited, Genetic Toxicology laboratories Study No. 881320, June 24, 1988. Negative response at 1000, 2000, 3000, 4000, 5000, and 8000 ug/plate.

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B. Salmonella/Mammalian-microsome mutagenicity test with CGA-154281 tech. (Lot. No. FL870211; DMSO as solvent). Ciba-Geigy Limited, Genetic Toxicology Laboratories Study No. 881321, June 24, 1988. Negative response at 1000, 2000, 3000, 4000, 5000, and 8000 ug/plate.

3. The submitted addendum (Accession No. 407321-02) provided adequate information concerning the identified impurities found in the materials (i.e., Batch Nos. 510001 and FL860318) which were initially synthesized in Switzerland and the modifications of the production process used to remove such impurities from commercial material in the United States. Toxicology Branch agrees with the confirmatory test results that the CGA-154281 technical should be synthesized by the modified production process only. Toxicology Branch defers to DEB the assessment of the modified production process for CGA-154281 technical.